Germline development in rat revealed by visualization and deletion of Prdm14.

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Authors: Toshihiro Kobayashi, Hisato Kobayashi, Teppei Goto, Tomoya Takashima, Mami Oikawa, Hiroki Ikeda, Reiko Terada, Fumika Yoshida, Makoto Sanbo, Hiromitsu Nakauchi, Kazuki Kurimoto, Masumi Hirabayashi

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Public Summary:
Primordial germ cells (PGCs), the founder cells of the germline, are specified in pre-gastrulating embryos in mammals, and subsequently migrate towards gonads to mature into functional gametes. Studying PGC specification and development is important for understanding the fundamentals of cell fate determination as well as the mechanisms underlying disease and infertility. Here, we investigated PGC development in rats, by genetically modifying Prdm14, a unique marker and an essential PGC transcriptional regulator. We traced PGC development in rats, for the first time, from specification until the sex determination stage in fetal gonads using Prdm14 H2BVenus knock-in rats. We uncovered that the crucial role of Prdm14 in PGC specification is conserved between rat and mice, by analyzing Prdm14-deficient rat embryos. Notably, loss of Prdm14 completely abrogates the PGC program, as demonstrated by failure of the maintenance and/or activation of germ cell markers and pluripotency genes. Finally, we profile the transcriptome of the post-implantation epiblast and all PGC stages in rat to reveal enrichment of distinct gene sets at each transition point, thereby providing an accurate transcriptional timeline for rat PGC development. These findings contribute to our understanding of how PGCs are generated during development and will inform efforts to generate them from pluripotent stem cells.

Scientific Abstract:
Primordial germ cells (PGCs), the founder cells of the germline, are specified in pre-gastrulating embryos in mammals, and subsequently migrate towards gonads to mature into functional gametes. Here, we investigated PGC development in rats, by genetically modifying Prdm14, a unique marker and an essential PGC transcriptional regulator. We trace PGC development in rats, for the first time, from specification until the sex determination stage in fetal gonads using Prdm14 H2BVenus knock-in rats. We uncover that the crucial role of Prdm14 in PGC specification is conserved between rat and mice, by analyzing Prdm14-deficient rat embryos. Notably, loss of Prdm14 completely abrogates the PGC program, as demonstrated by failure of the maintenance and/or activation of germ cell markers and pluripotency genes. Finally, we profile the transcriptome of the post-implantation epiblast and all PGC stages in rat to reveal enrichment of distinct gene sets at each transition point, thereby providing an accurate transcriptional timeline for rat PGC development. Thus, the novel genetically modified rats and data sets obtained in this study will advance our knowledge on conserved versus species-specific features for germline development in mammals.